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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,520	04/11/2006	Odilio Alves-Filho	Q-88759	5364

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EXAMINER	
SAUCIER, SANDRA E	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,520	ALVES-FILHO ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are pending. Claims 1-7 are considered on the merits. Claims 8-13 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Claims 8-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected inventions. Election was made without traverse in Paper No. 8/18/08.

Enablement

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the intended use of the product made, *i.e.* to produce a transfusion fluid containing viable cells (page 3, second paragraph). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

nature of the invention

The invention is directed to a dry, storage stable anuclear blood cell composition which may be platelets or red cells, both of which are anuclear, for the disclosed purpose of storage until medical use for transfusion. The specification describes at length problems in the field of storage of blood products in hospitals and during military operations and the need for storage of blood products longer than is currently possible for use in transfusions. Thus, the disclosure contemplates the use of the product of the instantly examined process of making claims to be a transfusible product which means that the reconstituted product must contain sufficient and viable cells for its disclosed, intended use.

breadth of the claims

The claims under examination are directed to a process of impregnating any macromolecular particulate with an anuclear blood cell concentrate, drying at temperatures of -20 to 120°C.

amount of guidance and working examples

The guidance is slight. The working example is directed to the impregnation of a powdered red cell composition with a red cell concentrate and drying at a temperature of 4°C for 6 hours to a moisture content of about 8%. The dried product was stored under ambient conditions for more than 120 days and reconstituted with buffered saline. Evidence of "viability" presented is that after 5 minutes of exposure to the buffer, the suspension was seen to contain cells under a light microscope. What kind of cells seen, (as a red cell concentrate contains cells other than red cells), what percentage recovery of the number of original cells, and if the "cells" were capable of functioning for their intended purpose is not disclosed in the specification.

state of the prior art and unpredictability

Wolkers *et al.* [U] is a review of the state of the art of dry preservation of eukaryotic cells at the time of applicants filing.

Preservation of blood cells with retention of their ability to function has long been a goal of the medical community, especially a dry, shelf-stable preparation as explained on pages 2 and 3 of the specification and Wolkers *et al.* [U], abstract. Applicants have presented evidence of the fragility of platelets and red cells on page 2, with regard to freeze-drying, which is a drying technique employed with delicate and labile biologicals, see O'Fagain [X] (abstract). Even the gentle drying method of sublimation after freezing (freeze-drying) of platelets and red cells is fraught with difficulties. The identity, type and concentration of the protective molecules which must be present in order to retain viability of the cells has been a matter of empirical determination and is still not completely predictable (Wolkers *et al.* [U], section 2.2). One embodiment of applicants' invention is the freeze-drying of the anuclear cell impregnated particles made of macromolecules of an unspecified type. If the macromolecular particles are intended to function as the cryoprotectant, it is well known that not all molecules have cryoprotectant or even lyoprotectant properties (Wolkers *et al.* [U], section 2.2).

Wolkers *et al.* [U] state that drying of cells generally leads to massive damage of cellular proteins and membranes (page 535, Section 1). Sugars in high concentrations confers desiccation tolerance (1.1).

At the present time there are only two ways that are known for the dry preservation of anuclear blood cells. One of which is to intracellularly load the cells with a sugar, and in the presence of extracellular sugar, drying under vacuum and transformation into the glassy state (Wolkers *et al.*, section 2.2), the other is to gently fix the cells with glutaraldehyde prior to freeze-drying as done by Read *et al.*, (Wolkers *et al.*, page 538). There is no known prior art using extreme ranges of temperatures as is instantly disclosed (-20 to 120°C) or the use of a fluidized bed for drying with retention of viability of a cell.

The instant method, which is discloses as drying over a range of temperatures in a fluidized bed dryer, without the presence of high concentrations of lyoprotectants which can form a glassy matrix (Wolkers *et al.*, section 2.2) and without crosslinking stabilization, appears to be at the frontier of the art of dry preservation of red cells and platelets with retention of viability. That which is new cannot be predictable, especially in a field where the need for such an invention has long been recognized (Wolkers *et al.*, abstract) and work on such an invention is well documented.

Platelet "viability" means the ability to function as a platelet, i.e., release of growth factors at the proper time and place and hemostatic properties, none of which are demonstrated to have survived applicants' preparation process, see Kiraly *et al.* [V], for a list of some of the *in vitro* tests which indicate platelet viability (abstract).

Red cell "viability" means the ability to function as a red cell, i.e. binding and release of oxygen or deformability which is a membrane property necessary for red cell circulation, see Podlosky *et al.* [W], for a listing of some of the *in vitro* tests which indicate red cell viability (abstract).

It has not been demonstrated by the specification that a red cell or platelet containing product, which can be exposed to temperatures up to 120°C, in an oxidizing environment (fluidized bed), can be reconstituted to produce a viable cell preparation which may be useful in transfusions as is instantly described in the generic portion of the specification. The viability of such a product has not been tested even *in vitro*, except for the merest of descriptions, involving viewing with a light microscope. Not even a determination of free hemoglobin is presented, which is basic indicator of hemolysis or any other parameter related to red cell viability, or a percentage of intact red cells recovered has been demonstrated in the sole exemplification. Seeing a few unidentified cell-like blebs under a microscope is not considered to be sufficient criteria for a viable cell preparation which may be useful as a transfusible composition.

Thus, applicant fails to teach how to use the invention for its intended purpose because the viability of the dry-preserved cells made by the process is not demonstrated and given the teachings of the state of the art, it is highly doubtful that the composition possess sufficient cell viability and number to be even hopefully useful for its intended purpose given the current state of the art and knowledge of those of skill in the art of dry preservation of platelets, red cells and other delicate biologicals.

Undue experimentation would be required to practice the invention due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5,432,097 [A].

The claims are directed to a process for the preparation of a dried particulate anuclear blood cell product comprising:

obtaining a blood sample,
adding an anticoagulant to the sample,
concentrating the cells of the sample,
recovering the concentrate,
impregnating a particulate comprising a macromolecular protective material,
drying the impregnated particulate at a temperature of -20 to 120°C, optionally packaging the material in sealed containers.

The reference is relied upon as explained below.

US 5,432,097 discloses a method comprising: obtaining blood from a human, anticoagulating the blood, concentrating the blood and removing the buffy coat, impregnating paper, which contains particulate cellulose, with the concentrate, drying at room temperature, storing in plastic bags, (col. 3, ls. 20-65).

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting

claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner
Art Unit 1651